

AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A pharmaceutical composition comprising
 - i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO:14), wherein said at least one peptide fragment is less than 90% of the length of said N2 sequence, and wherein X represents an amino acid, or a retro-inverso form of said at least one peptide, and
 - ii) [[and]] a genotoxin,wherein said at least one peptide fragment enhances the ability of said genotoxin to kill selectively cancer cells.
2. (Previously Presented) The pharmaceutical composition of claim 1, wherein said at least one peptide fragment comprises at least one amino acid sequence encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, and SEQ ID NO:4.
3. (Previously Presented) The pharmaceutical composition of claim 1, wherein said at least one peptide fragment comprises the amino acid sequence WMWVTNLRD (SEQ ID NO: 8).
4. (Previously Presented) The pharmaceutical composition of claim 1, wherein said at least one peptide fragment further comprises at least one amino acid in D-form.
5. (Previously Presented) The pharmaceutical composition of claim 1, wherein said at least one peptide fragment is further conjugated to an agent which increases the cell accumulation of said at least one peptide fragment.
6. (Previously Presented) The pharmaceutical composition of claim 5, wherein the agent is a cell membrane permeable carrier.
7. (Previously Presented) The pharmaceutical composition of claim 6, wherein the cell membrane permeable carrier is a peptide.

8. (Previously Presented) The pharmaceutical composition of claim 7, wherein the cell membrane permeable carrier peptide comprises at least one amino acid in D-form.
9. (Previously Presented) The pharmaceutical composition of claim 7, wherein the cell membrane permeable carrier peptide is an arginine rich peptide which is selected from the group consisting of an HIV-TAT₄₈₋₅₇ peptide (SEQ ID NO:15), an FHV-coat₃₅₋₄₉ peptide, an HTLV-II Rex₄₋₁₆ peptide, and a BMV gag₇₋₂₅ peptide.
10. **(Canceled)**
11. (Previously Presented) The pharmaceutical composition of claim 1, wherein the genotoxin is selected from the group consisting of an alkylating agent, an antimetabolite, a DNA cutter, a DNA binder, a topoisomerase poison, and a spindle poison.
12. (Previously Presented) The pharmaceutical composition of claim 11, wherein said alkylating agent is selected from the group consisting of lomustine, carmustine, streptozocin, mechlorethamine, melphalan, uracil nitrogen mustard, chlorambucil, cyclophamide, iphosphamide, cisplatin, carboplatin, mitomycin, thiotepa, dacarbazine, procarbazine, hexamethyl melamine, triethylene melamine, busulfan, pipobroman, mitotane, and other platinum compounds.
13. **(Canceled)**
14. (Previously Presented) The pharmaceutical composition of claim 48, wherein the DNA cutter is bleomycin.
15. (Previously Presented) The pharmaceutical composition of claim 49, wherein the topoisomerase poison is selected from the group consisting of topotecan, irinotecan, camptothecin sodium salt, daorubicin, doxorubicin, idarubicin, mitoxantrone, teniposide, adriamycin, and etoposide.
16. **(Canceled)**

17. (Previously Presented) The pharmaceutical composition of claim 50, wherein the DNA binder is dactinomycin or mithramycin.

18. (Previously Presented) The pharmaceutical composition of claim 51, wherein the spindle poison is selected from the group consisting of vinblastin, vincristin, navelbin, paclitaxel, and docetaxel.

19. (Previously Presented) The pharmaceutical composition of claim 52, wherein the antimetabolite is selected from the group consisting of methotrexate, trimetrexate, pentostatin, cytarabin, ara-CMP, fludarabine phosphate, hydroxyurea, fluorouracyl, floxuridine, chlorodeoxyadenosine, gemcitabine, thioguanine, and 6-mercaptopurine.

20-22. **(Canceled)**

23. (Previously Presented) The method according to claim 40, wherein the cancer is selected from the group consisting of carcinoma, lymphoma, blastoma, sarcoma, liposarcoma, neuroendocrine tumor, mesothelioma, schwannoma, meningioma, adenocarcinoma, melanoma, leukemia, lymphoid malignancy, squamous cell cancer, epithelial squamous cell cancer, lung cancer, small-cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung, squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastric or stomach cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, rectal cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney or renal cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma, anal carcinoma, penile carcinoma, testicular cancer, esophageal cancer, a tumor of the biliary tract, and head and neck cancer.

24-26. **(Canceled)**

27. (Previously Presented) A method for enhancing apoptosis selectively in a cancer cell, comprising contacting a cancer cell with a therapeutically effective amount of the pharmaceutical composition of claim 1.

28. (Previously Presented) A method for selectively killing cancer cells comprising contacting a cancer cell with a therapeutically effective amount of the pharmaceutical composition of claim 1.

29. (Currently Amended) A kit for treating cancer in a subject comprising a pharmaceutical composition comprising

i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO:14), wherein X represents an amino acid, or a retro-inverso form of said at least one peptide, and

ii) [[and]] a genotoxin,

wherein said at least one peptide fragment enhances the ability of said genotoxin to kill selectively cancer cells, and instructions for use.

30. (Previously Presented) The kit of claim 29, further comprising a separate pharmaceutical dosage form including an additional anti-cancer agent selected from the group consisting of drugs, anti-epidermal growth factor receptors antibodies, radioimmunotherapeutic agents, and combinations thereof.

31. (Currently Amended) A kit for treating cancer in a subject comprising

i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO:14), wherein X represents an amino acid; or a retro-inverso form of said at least one peptide, and

ii) a genotoxin,

wherein said at least one peptide fragment enhances the ability of said genotoxin to kill selectively cancer cells, and instructions for use of said at least one peptide fragment and the genotoxin.

32. (Previously Presented) The kit of claim 31, further comprising a genotoxin.

33. (Currently Amended) A method for enhancing apoptosis in a cancer cell, comprising contacting the cancer cell with a therapeutically effective amount of

i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO:14), wherein said at least one peptide fragment is less than 90% of the length of said N2 sequence, and wherein X represents an amino acid, or a retro-inverso form of said at least one peptide, and

ii) a genotoxin,

wherein said at least one peptide fragment enhances the ability of said genotoxin to selectively kill said cancer cell.

34. (Previously Presented) The method of claim 33, wherein said at least one peptide fragment comprises the SH3 domain of the N2 sequence, or a part thereof, or comprises at least one amino acid sequence encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, and SEQ ID NO:4.

35. (Previously Presented) The method of claim 33, wherein the genotoxin is selected from the group consisting of an alkylating agent, an antimetabolite, a DNA cutter, a DNA binder, a topoisomerase poison, and a spindle poison.

36. (Previously Presented) The method of claim 33, wherein the genotoxin is selected from the group consisting of cisplatin, mitoxantrone and adriamycin.

37. (Currently Amended) A method for enhancing the sensitivity of a cancer cell to a genotoxin comprising contacting the cancer cell with a genotoxin and a therapeutically effective amount of at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO:14), wherein said at least one peptide fragment is less than 90% of the length of said N2 sequence, and wherein X represents an amino acid, or a retro-inverso form of said at least one peptide, thereby enhancing the sensitivity of a cancer cell to the genotoxin.

38. (Previously Presented) The method of claim 37, wherein said at least one peptide fragment comprises the SH3 domain of the N2 sequence, or a part thereof, or comprises at least one amino acid sequence encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, and SEQ ID NO:4.
39. (Previously Presented) The pharmaceutical composition of claim 1, wherein said at least one peptide fragment comprises the SH3 domain of the N2 sequence, or a part thereof.
40. (Currently Amended) A method of treating cancer in a subject comprising administering to said subject a therapeutically effective amount of
- i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO:14), wherein X represents an amino acid, or a retro-inverso form of said at least one peptide, and
 - ii) a genotoxin,
- wherein said at least one peptide fragment enhances the ability of said genotoxin to kill selectively cancer cells, such that said cancer is treated.
41. (Previously Presented) The method of claim 40, wherein said at least one peptide fragment comprises the SH3 domain of the N2 sequence, or a part thereof, or comprises at least one amino acid sequence encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, and SEQ ID NO:4.
42. (Previously Presented) The method of claim 40, wherein the genotoxin is selected from the group consisting of an alkylating agent, an antimetabolite, a DNA cutter, a DNA binder, a topoisomerase poison, and a spindle poison.
43. (Previously Presented) The method of claim 40, wherein the genotoxin is selected from the group consisting of cisplatin, mitoxantrone and adriamycin.
44. (Previously Presented) The pharmaceutical composition of claim 4, wherein said D-form amino acids are in retro-inverso form.

45. (Previously Presented) The pharmaceutical composition of claim 8, wherein said D-form amino acids are in retro-inverso form.

46. (Previously Presented) The pharmaceutical composition of claim 1, wherein said at least one peptide fragment comprises at least one amino acid in retro-inverso form.

47. (Previously Presented) The pharmaceutical composition of claim 7, wherein said at least one peptide fragment comprises at least one amino acid in retro-inverso form.

48. (Currently Amended) A pharmaceutical composition comprising

i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO:14), wherein said at least one peptide fragment is less than 90% of the length of said N2 sequence, and wherein X represents an amino acid, or a retro-inverso form of said at least one peptide, and

ii) [[and]] a genotoxin, wherein said genotoxin is a DNA cutter, and wherein said at least one peptide fragment enhances the ability of said genotoxin to kill selectively cancer cells.

49. (Currently Amended) A pharmaceutical composition comprising

i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO:14), wherein said at least one peptide fragment is less than 90% of the length of said N2 sequence, and wherein X represents an amino acid, or a retro-inverso form of said at least one peptide, and

ii) [[and]] a genotoxin, wherein said genotoxin is a topoisomerase poison, and wherein said at least one peptide fragment enhances the ability of said genotoxin to kill selectively cancer cells.

50. (Currently Amended) A pharmaceutical composition comprising

i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO:14), wherein said at least one peptide fragment is less than 90% of the length of said N2 sequence, and wherein X represents an amino acid, or a retro-inverso form of said at least one peptide, and

ii) [[and]] a genotoxin, wherein said genotoxin is a DNA binder, and wherein said at least one peptide fragment enhances the ability of said genotoxin to kill selectively cancer cells.

51. (Currently Amended) A pharmaceutical composition comprising

i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO:14), wherein said at least one peptide fragment is less than 90% of the length of said N2 sequence, and wherein X represents an amino acid, or a retro-inverso form of said at least one peptide, and

ii) [[and]] a genotoxin, wherein said genotoxin is a spindle poison, and wherein said at least one peptide fragment enhances the ability of said genotoxin to kill selectively cancer cells.

52. (Currently Amended) A pharmaceutical composition comprising

i) at least one peptide fragment of the N2 sequence of the RasGAP protein which comprises the amino acid sequence WXWVTXXRTX (SEQ ID NO:14), wherein said at least one peptide fragment is less than 90% of the length of said N2 sequence, and wherein X represents an amino acid, or a retro-inverso form of said at least one peptide, and

ii) [[and]] a genotoxin, wherein said genotoxin is an antimetabolite, and wherein said at least one peptide fragment enhances the ability of said genotoxin to kill selectively cancer cells.

53. (Previously Presented) The pharmaceutical composition of claim 1, wherein said at least one peptide fragment is less than 60% of the length of said N2 sequence.

54. (Previously Presented) The pharmaceutical composition of claim 1, wherein said at least one peptide fragment is less than 30% of the length of said N2 sequence.

55. (Previously Presented) The pharmaceutical composition of claim 29, wherein said at least one peptide fragment is less than 90% of the length of said N2 sequence.

56. (Previously Presented) The pharmaceutical composition of claim 29, wherein said at least one peptide fragment is less than 60% of the length of said N2 sequence.

57. (Previously Presented) The pharmaceutical composition of claim 29, wherein said at least one peptide fragment is less than 30% of the length of said N2 sequence.

58. (Previously Presented) The pharmaceutical composition of claim 31, wherein said at least one peptide fragment is less than 90% of the length of said N2 sequence.

59. (Previously Presented) The pharmaceutical composition of claim 31, wherein said at least one peptide fragment is less than 60% of the length of said N2 sequence.

60. (Previously Presented) The pharmaceutical composition of claim 31, wherein said at least one peptide fragment is less than 30% of the length of said N2 sequence.

61. (Previously Presented) The pharmaceutical composition of claim 33, wherein said at least one peptide fragment is less than 60% of the length of said N2 sequence.

62. (Previously Presented) The pharmaceutical composition of claim 33, wherein said at least one peptide fragment is less than 30% of the length of said N2 sequence.

63. (Previously Presented) The pharmaceutical composition of claim 40, wherein said at least one peptide fragment is less than 90% of the length of said N2 sequence.

64. (Previously Presented) The pharmaceutical composition of claim 40, wherein said at least one peptide fragment is less than 60% of the length of said N2 sequence.

65. (Previously Presented) The pharmaceutical composition of claim 40, wherein said at least one peptide fragment is less than 30% of the length of said N2 sequence.